UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,863	01/15/2004	Leonard Presta	P1726R1D1	5958

9157 7590 01/25/2008

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

MAIL DATE	DELIVERY MODE
01/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/757,863	PRESTA, LEONARD	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *24* is/are allowed.

6)☒ Claim(s) *19,21 and 22* is/are rejected.

7)☒ Claim(s) *20 and 23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/06/07 and 11/14/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment to the claims, filed on November 6, 2007, is acknowledged.

Claims 1-18 have been previously canceled.

Claims 22-24 have been added.

Claims 19-24 are pending.

Newly added claims 21 and 23 encompass nonelected species because claims 21 and 23 are drawn to a method for treating lymphoma by using an antibody comprising a variant Fc region comprising one or more amino acid substitutions at positions in addition to the originally elected amino acid substitution at positions 298, 333, and 334. These species are distinct because antibodies comprising Fc variants comprising amino acid substitutions at different residues differ with respect to structures, physicochemical properties and mode of action.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by the original presentation for prosecution on the merits.

Accordingly, claims 19-24 are currently under consideration as they read on the originally elected invention of a method for treating lymphoma in a mammal comprising administering a therapeutically effective amount of a variant of a parent anti-CD20 antibody comprising an variant Fc region comprising amino acid substitutions at position 298, 333, and 334.

2. This Office Action will be in response to applicant's arguments, filed on November 6, 2007.

The rejections of record can be found in the previous Office Actions mailed on October 11, 2005, May 22, 2006, and July 6, 2007.

3. Applicant's IDSs, filed on November 6, 2007 and November 14, 2007, have been considered.

4. Claims 20 and 23 are objected for following reasons:

A) Claim 20 is objected to as being dependent upon a rejected base claim 19 but would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. 112, first paragraph, set forth in this Office action.

B) Claim 23 is objected to because the claim encompasses nonelected species.

5. In view of applicant's amendment to the claims, only the following rejections have been maintained.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims19 and newly added claim 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating lymphoma by administering a variant anti-CD20 antibody and comprises an Fc region which mediates ADCC more effectively than the parent antibody and comprises amino acid substitution in the Fc region at positions 298, 333, and 334, does not reasonably provide enablement for said method by administering a variant anti-CD20 antibody comprising "at least one amino acid substitution in the Fc region" and/or "two or more amino acid substitutions in the Fc region". The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's argument, filed on November 6, 2007, has been fully considered but has not been found persuasive.

Applicant argues that although the preferred embodiment of the invention is a variant with amino acid substitutions at positions 298, 333 and 334 of the Fc region, many residues in the Fc region can be modified to make variants for improved ADCC; applicant further asserts that there are numerous working examples of the Fc variants. Furthermore, applicant argues that the specification discloses how to make additional variants for improved ADCC function using screening methods; as such applicant asserts that one of skill in the art would be able to practice the claimed invention following the teachings of the instant specification. Moreover, applicant asserts that the anti-CD20 antibody comprising Fc variant are efficient for in vivo application as demonstrated in US patent application US2006/024600 (reference 208 on IDS). In addition, applicant argues that similar claims not reciting specific amino acid residues and positions have been granted in US Patent 6,737,056. Therefore, applicant asserts that the claimed method for treating lymphoma by administering an anti-CD20 antibody comprising at least one amino acid substitution in the Fc region is enabled.

This is not found persuasive for following reasons:

In contrast to applicant's assertion that the claimed method is enabled, it is noted that there are 218 amino acid residues in the Fc region (e.g. see Figure 22A and page 11 of the instant specification). While the instant specification discloses specific amino acid substitutions at specific positions of the Fc region, the instant claims encompasses in their breath any anti-CD20 antibody comprising "at least one amino acid substitution in the Fc region" and/or "two or more amino acid substitutions in the Fc region". Therefore, the disclosure of specific amino acid substitutions at specific positions of the Fc region is insufficient in providing guidance and direction for the instant claims.

Further, in contrast to applicant's reliance on screening method for making Fc variant with improved ADCC function, it is noted that tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. See Genentech, Inc. v. Novo Nordisk A/S 42 USPQ2d 1001, 1005 (Fed. Cir. 1997) quoting In re Wright, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Further, the reference applicant is relying on for support (US patent application US2006/024600, reference 208 on IDS) teaches in vivo efficacy of anti-CD20 antibody variant comprising specific amino acid substitutions at specific positions of the Fc region, e.g. S298A, E333A, and K334A; therefore, the reference does not support methods of treating lymphoma by administering anti-CD20 antibody comprising random substitutions in the Fc regions and random combinations of such substitutions.

Moreover, regarding applicant's argument that similar claims not reciting specific amino acid residues and positions have been granted in US Patent 6,737,056, it is noted that it is well settled that whether similar claims have been allowed to others is immaterial. See In re Giolito, 530 F.2d 397, 188 USPQ 645 (CCPA 1976) and Ex parte Balzarini 21 USPQ2d 1892, 1897 (BPAI 1991).

In this case, the claims that have been issued to US Patent 6,737,056 are immaterial to the instant application. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

In view of the quantity of experimentation necessary, the limited working example, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 19, 21, and newly added claim 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Idusogie et al. (US Patent 6,528,624, claims priority to provisional USSN 60/080,447 filed on April 2, 1998. Reference 16 on IDS filed on October 11, 2005) for reasons of record set forth in the Office Action mailed October 11, 2005, May 22, 2006 and July 6, 2007 as evidenced by Reff et al. (Blood 1994, 83;2:435-445, reference 129 on IDS) and Presta (US Patent 6,737,056, reference 176 on IDS).

Applicant's argument has been fully considered but has not been found persuasive.

Applicant argues that the instant claims are drawn to a method of treating lymphoma; while the prior art Idusogie et al. teaches methods of treating cancer. Therefore, applicant asserts that the prior art does not anticipate the claimed invention. Further, applicant argues that Idusogie et al. claim priority to USSN 60/080,477 that only has support for Fc variant comprising amino acid substitution at position 334 of the Fc region and since Fc variant comprising K334 shows little or no effect on C1q binding, said Fc variant would not be chosen for treatment. Thus, applicant argues that the rejection should be withdrawn.

This is not found persuasive for following reasons:

Contrary to applicant's assertion that Idusogie et al. only teach methods of treating cancer but not treating lymphoma, it is noted that Idusogie et al. teach methods of treating cancer by using anti-CD20 antibody (e.g. see columns 10 and column 19); further, Idosogie et al. provided working example of constructing antibody comprising Fc variants using a well-known chimeric anti-CD20 antibody C2B8 from Reff et al. (Blood 1994, 83;2:435-445, reference 129 on IDS). As evidenced by Reff et al, it was well-know in the art at the time of invention that antibody C2B8 can be used to treat B-cell lymphoma (e.g. see abstract). Therefore, although Idusogie et al. do not specifically name the species of lymphoma, one of ordinary skill in the art is able to at once envisage that the specific cancer, which an anti-CD20 antibody comprising Fc variant can be used to treat, is lymphoma. Therefore, the teachings of Idusogie et al. meet the claimed limitation of method of treating lymphoma.

Further, in contrast to applicant's assertion that the prior art antibody comprising substitution at position 334 of the Fc region would not be chosen for treatment due to little or no effect on C1q binding, it is noted that Idusogie et al. teach that even the Fc variants that do not bind C1q can be used for the methods of treating diseases as long as the Fc variants maintain their ability to bind Fc gamma receptors (e.g. see column 5). Thus, the prior art teachings would anticipate claims 19 and 21 that encompassing a method of treating lymphoma using anti-CD20 antibody comprising at lest one amino acid substitution in the Fc region because the prior art teaches the same method as claimed by using anti-CD20 antibody comprising substitutions in positions such as 334.

Furthermore, newly added claim 22 is included in this rejection because Idusogie et al. teach two or more amino acid substitutions in the Fc regions at positions such as 322 and 331 (e.g. see column 5) and as evidenced by Presta, modification at positions 322 and 331 of the Fc region would produce an Fc variant with improved binding to the Fc receptors (e.g. see column 23). Therefore, it would have been inherent properties of the prior art antibody comprising two or more amino acid substitutions in the Fc region to have improved ADCC function.

Therefore, applicant's argument has not been found persuasive.

10. Claim 24 is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is 571-272-8142. The examiner can normally be reached on 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Larry Helms can be reached 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Chun Crowder
Patent Examiner
January 9, 2008

Maher M. Haddad
MAHER M. HADDAD
PRIMARY EXAMINER